SECTION 1: Headlines overview

- Electrical & chemical changes during action potential in nerve fiber
- Impulse propagation
- Theories of how L.A. work
- Dissociation of L.A
- Kinetics of L.A.
- Chemical structure classification of L.A.
- Pharmacology of L.A.
- Pharmacology of vasoconstrictors
- Indications & contraindications of L.A.& vasoconstrictor
- Pain & pain pathway from oral & maxillofacial region

The resting state

In the resting state the membrane is

- Slightly permeable to sodium ions (Na +)
- Freely permeable to potassium ions (Ka +)
- Freely permeable to chloride ions (Cl -)

Membrane excitation

Depolarization :

- Excitation of nerve segment leads to increase of membrane permeability to sodium ions
- This is accomplished through widening of the transmembrane ion channels sufficient to permit unhindered passage of hydrated sodium ions
- This rapid influx of sodium ions to the interior of the cell membrane causes depolarization of the cell membrane
- A decrease in the negative trans- membrane potential of 15 mV i.e. from -70 mV to -55 mV) is required to reach the firing threshold
- When the firing threshold is reached permeability of the membrane to sodium ions increase dramatically to lead to reversal of electrical potential reaching +40 mV requiring 0.3 msec to occur

Repolarization
- Extinction of the increased permeability to sodium
- In many cells permeability to potassium also increases leading to efflux of K+ and more rapid repolarization and return to resting potential

Impulse propagation
- Local currents
- Reversal of polarity in adjacent segment
- Firing threshold
- Action potential
- The entire process starts anew

Impulse spread
- Unmyelinated nerve fiber
- Myelinated nerve fiber

Membrane expansion theory
Specific receptor theory

Dissociation of local anesthesia
Why no L.A.in acute inflammation

Kinetics of L.A.:
- Induction time
- Physical properties & clinical actions:
    - pKa (dissociation constant)
    - Lipid solubility
    - Protein binding
    - Vasoactivity
- Recovery from block anesthesia
- Tachyphylaxis
- Duration of L.A.

CHEMICAL STRUCTURE CLASSIFICATION OF L.A.

AMIDE GROUP LOCAL ANESTHETICS

- Articaine
- Bupivacaine (long acting)
- Dibucaine
- Etidocaine (long acting)

- Lidocaine (moderate acting)
- Mepivacaine (moderate acting)
- Prilocaine (moderate acting)

PHARMACOLOGY OF L.A.

- Distribution

- Factors governing level of L.A. in the blood:
- The rate at which it is absorbed
- The rate of distribution into tissues
- The rate of metabolism & excretion

- THE HALF-LIFE

METABOLISM OF L.A.

- ESTERS
  - Atypical pseudocholinesterase
- AMIDES
- Biotransformation products.eg.
- Excretion

SYSTEMIC ACTIONS OF L.A.

- CNS

- CVS

- DRUG INTERACTIONS

PHARMACOLOGY OF VASOCONSTRICTORS

Advantages of using vasoconstrictor

- Decreasing amount of local anesthesia absorbed into the circulation

- Decreasing the risk of anesthetic toxicity

- Prolonging the anesthetic duration

- Decreasing the bleeding anticipated in the operative field specially during surgical procedures

Adrenergic receptors

- α (alpha) receptors : subtypes:

- α 1 : excitatory postsynaptic
- α 2 : inhibitory postsynaptic

- β (beta) receptors : subtypes:
- β 1 : found in the heart & small intestine
- β 2 : found in the bronchi & vascular bed & uterus

Epinephrine (adrenalin)

- Action : acts on both α & β receptors with β effects predominant

- Systemic actions:
- Myocardium:
- positive inotropic effect (cardiac output) & positive chronotropic effect (heart rate)
- Pacemaker cells:
- increases irritability of pace maker cells leading to dysrythmias, ventricular tachycardia, & premature ventricular contractions

- Coronary arteries:
- increase coronary blood flow
- Blood pressure:
- Systolic increases while diastolic decreases at small doses administration. At larger dose diastolic increases
- Cardiovascular dynamics:
- Increase systolic & diastolic pressures, cardiac outputs, stroke vol., heart rate, myocardial contractility, and oxygen consumption

- Vascular bed:
- Primarily act on small arterioles & precapillary sphincters. Vessels of skin mucous membrane & kidney contain α receptors. Skeletal muscles contain both α & β 2 receptors
- Respiratory system:
- Potent bronchodilator through β 2 effect
- CNS:
- Stimulation at highly excessive doses

- Metabolism:

- Through β effect glycogenolysis in liver & skeletal muscles leads to high blood sugar level , about 4 carpules of 1:100000 adrenalin are needed to elicit this action

- Termination of action & elimination:
- Primarily by reuptake at adrenergic nerves
- Adrenalin escaping uptake is inactivated by (COMT) & (MAO) present in the liver.1% is excreted unchanged in the urine

Clinical applications

- Acute allergic reactions
- Bronchspasm
- Cardiac arrest
- Local hemostasis as vasoconstrictor
- With local anesthesia to prolong action & decrease its absorption into the circulation
- Availability in dentistry:
- 1:50000 with lidocaine
- 1:100000 with articaine
lidocaine
mepecaine
- 1: 200000 with articaine
lidocaine
etidocaine
bupivacaine
mepevacaine
prilocaine

CONCENTRATION OF VASOCONSTRICTOR

- 1:100,000 adrenaline means
- 1 gm / 100,000 ml = 1000mg/ 100,000 ml
- As maximum doses should always be presented in mg or more commonly nowadays in µg So.
- 1mg/100ml=0.01mg/ml (0.018mg /1carpule)

- or 10 µg/ml (18µg/1carpule)
- Maximum doses:

- Normal healthy patient 0.2 mg / appointment

- Patient with clinically significant cardiovascular disease (ASA III OR ASA IV)
  0.04 mg / appointment

Levonordefrin (Neo-cobefrin)
- Mode of action:
- Direct α action (75%) & some β activity (25%)
- It is 15 % as potent a vasopressor as epinephrine
- Systemic actions: the same as epinephrine on myocardium, pacemaker, coronary vessels, heart rate, vascular bed, respiratory system, CNS, & metabolism but to a lesser degree
- Termination of action & elimination:
- Through actions of COMT & MAO

- Clinical applications:
- As vasoconstrictor in local anesthetics

- Availability in dentistry: 1:20000 with mepevacaine,propoxycaine / or procaine

- Maximum dose: 1 mg / appointment

Norepinephrine (Levarterenol)
- Mode of action:
- Exclusively on α receptors (90%) but also has β actions in the heart (10%)
- It is one fourth as potent as epinephrine

- Systemic actions:
- Myocardium:
- Positive inotropic effect

- Pacemaker: as epinephrine
- Heart rate:

- Decrease in heart rate caused by reflex action of the aortic & carotid baroreceptors & the vagus nerve following a marked increase in both systolic & diastolic pressures

- Blood pressure: increase in both systolic & diastolic pressures with the systolic to a greater extent
- Vascular bed:
- Constriction of cutaneous vessels and rise of total peripheral resistance & both systolic & diastolic pressure

- CNS: the same as epinephrine with overdose

- Metabolism: increase BMR & tissue oxygen consumption & increase in blood sugar
- Cardiovascular dynamics:
- Overall action is:
- Increase in both systolic & diastolic pressure
- Increased stroke volume
- Increased total peripheral resistance
- Decreased heart rate
- Unchanged or slightly decreased cardiac output
- Termination of action & elimination:
- Reuptake at adrenergic nerve terminals & oxidation by MAO. Exogenous norepinephrine is inactivated by COMT

- Clinical applications:
- Treatment of hypotension
- Vasoconstrictor in local anesthetics
- Availability in dentistry:
- 1:30000 with procaine & propoxycaine in US
- With lidocaine & mepivacaine in Germany
- Combination of epinephrine & norepinephrine with lidocaine in Germany or tolycaine in Japan

- Maximum doses:
- Normal healthy patient: 0.34 mg / appointment (10 ml of 1:30000)

- Patient with clinically significant CV disease (ASA III 0R IV) 0.14MG / appointment (approx. 4 ml of 1:30000)

Phenylephrine hydrochloride
(neo-synephrine)

- Mode of action: mostly direct α receptor stimulation (95%) the effect is less but the duration is longer. It is only 5% as potent as epinephrine

- Systemic actions:
- Myocardium & pacemaker: very little effect
- Coronary arteries: increased blood flow
- Blood pressure: increase in both systolic & diastolic pressures

- Heart rate: bradycardia due to reflex action
- Cardiovascular dynamics: almost as norepinephrine
- Respiratory system: bronchodilator but to a lesser degree than epinephrine
- CNS: minimum effect
- Metabolism: some increase in BMR & glycogenolysis as epinephrine

- Termination of action & elimination:
- Hydroxylation to epinephrine the oxidation to metanephrine then eliminated in the same manner as epinephrine
- Clinical application:
- Vasoconstrictor in local anesthesia
- Management of hypotension
- Nasal decongestant
- Availability in dentistry:
- With 4% procaine in 1:2500 dil.

- Maximum doses:
- Normal healthy patient: 4 mg / appiontment
- Patient with clinically significant CV impairment (ASA III OR IV) 1.6 mg / appt.

Felypressin (octapressin)

- Mode of action: on the direct smooth muscle mostly on the venous than the arterial microcirculation

- Systemic actions:
- Myocardium: no direct effect
- Pacemaker: non dysrythmogenic
- Coronary arteries: impair blood flow in greater than therapeutic dose
- Vascular bed: in higher than therapeutic doses constriction of cutaneous vessels may cause facial pallor

- CNS: it has no effect on adrenergic nerve transmission so it is safe with hyperthyroid patients, any one receiving MAO inhibitors, or tricyclic antidepressants

- Uterus: it has oxytocic effect so not used in pregnancy
- Clinical application: as vasoconstrictor in local anesthesia

- Availability in dentistry: 0.03 IU/ml with 3% prilocaine in Japan & Germany

- Maximum doses:
- Patients with clinically significant CV impairment (ASA III OR IV) 0.27 IU

The selection of vasoconstrictor

- Factors taken into consideration:
- The duration needed

- Need for hemostasis

- Need for postoperative pain control

- Medical status of the patient